

Multiple Sebaceous Tumors May Show Syndrome

The patient's new tumors were found to be sebaceous adenomas, raising the possible diagnosis of Muir-Torre syndrome.

Family history revealed that his brother, who was 2 years older, had undergone a hemicolectomy for adenocarcinoma several years earlier. The brother was called in for examination and was found to have a number of tiny, crust-covered tumors on his back and face that resembled sebaceous gland tumors.

Both of his sisters had had surgery for gynecologic cancers; one had died 2 years earlier of ovarian cancer. His mother also had died of an undetermined gynecologic cancer.

After excision, the patient's new tumors were found to be sebaceous adenomas, a result that raised the possibility that this patient and his family members had Muir-Torre syndrome, said Dr. Gaspar of the department of dermatology at Medical and Health Science Center, University of Debrecen (Hungary).

Muir-Torre syndrome is a rare dermatosis that exhibits an autosomal dominant inheritance pattern. The syndrome, which is characterized by sebaceous lesions and visceral malignancies, is considered a phenotypic variant of hereditary nonpolyposis colorectal cancer. Both conditions are caused by inherited DNA mismatch repair defects, most commonly on the MSH2 and MLH1 genes.

Among the skin lesions characteristic of Muir-Torre syndrome are sebaceous adenomas, epitheliomas, and carcinomas. Adenomas appear as skin-colored or yellowish papules or nodules, sometimes with a central depression. Histologic evaluation in this case showed orthokeratotic, dilated follicles, numerous nucleioli, and a lack of sebium.

Sebaceous carcinoma appears as a poorly demarcated, asymmetrical, solid tumor with an irregular border. Histology showed that this lesion had deep penetrating tumor cell nests that obliterated the normal structure of the sebaceous gland.

This case illustrates the importance of a careful search for possibly asymptomatic abdominal tumors in the setting of multiple sebaceous tumors. Patients whose cutaneous tumor cells are genetically unstable (characterized by mutations of short DNA sequences known as microsatellites) also are at heightened risk for developing subsequent abdominal cancers. "Therefore, microsatellite screening can play a significant role in cancer prevention," Dr. Gaspar said.

In more than half of cases the visceral malignancy is colorectal carcinoma. Gastrointestinal, hematologic, and head and neck sites also have been reported.

Vigilance is necessary, and repeated surgeries for both skin and visceral tumors can be expected. Family members also will be evaluated and followed. But with careful follow-up, the prognosis of Muir-Torre syndrome is good, with 10-year survival exceeding 50%. Dr. Gaspar said at the symposium, also sponsored by the Hungarian Dermatological Society.

At the patient's most recent follow-up examination, his tumor markers were normal, but radiographic evaluation revealed metastases to the paraortic lymph nodes. He was started on a chemotherapeutic regimen that included irinotecan.

By Nancy Walsh
New York Bureau

COURTESY DR. ISTVAN JUHASZ

BUDAPEST, HUNGARY — A 56-year-old man with a 7-year history of multiple small cutaneous tumors histologically identified as basal cell carcinomas was found with new skin-colored tumors on his forehead and back. K. Gaspar, M.D., said at an international symposium sponsored by the European Academy of Dermatology and Venereology.

Hepatic Impairment

A study of OxyContin in patients with hepatic impairment indicates greater plasma concentrations than those with normal function. The initiation of therapy at 10 mg to 160 mg per day is recommended.

Renal Impairment

Patients with renal impairment, as evidenced by decreased creatinine clearance (<60 mL/min), the concentrations of oxycodone in plasma are approximately 25% higher than in subjects with normal renal function. Dose initiation should follow a conservative approach. Dosages should be adjusted according to the clinical response.

Gender Differences

In pharmacokinetic studies, opioid-naïve females demonstrated up to 25% higher average plasma concentrations and greater overall adverse events than males, even after adjustment for body weight. The clinical relevance of a difference of this magnitude is not clear for a drug intended for chronic use.

ADVERSE REACTIONS

The safety of OxyContin was evaluated in double-blind clinical trials involving 712 patients with moderate to severe pain of various etiologies. In open-label studies of cancer pain, 192 patients received OxyContin in total daily doses ranging from 20 mg to 640 mg per day. The average total daily dose was approximately 105 mg per day.

Serious adverse reactions which may be associated with OxyContin therapy in clinical use are those observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, and to an lesser degree, circulatory depression, hypotension, or shock (see WARNINGS). The non-serious adverse events seen on initiation of therapy with OxyContin are typical opioid side effects. These events are dose-dependent, and their frequency depends upon the dose, the clinical setting, the patient's level of opioid tolerance, and most factors specific to the individual. They should be expected and managed as a part of opioid analgesia. The most frequent (>5%) include constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, sweating, and asthenia. In many cases the frequency of these events during initiation of therapy may be minimized by careful individualization of starting dosage, slow titration, and the avoidance of large swings in the plasma concentration of the opioid. Many of these adverse events will cease or decrease in intensity as OxyContin therapy is continued and some degree of tolerance is developed.

Clinical trials comparing OxyContin with immediate-release oxycodone and placebo revealed a similar adverse event profile between OxyContin and immediate-release oxycodone. The most common adverse events (>5%) reported by patients at least once during therapy were:

Table with 3 columns: OxyContin (n=227), Immediate-Release (n=226), and Placebo (n=45). Rows list adverse events like Constipation, Nausea, Somnolence, Dizziness, Pruritus, Vomiting, Headache, Dry Mouth, Asthenia, and Sweating.

The following adverse experiences were reported in OxyContin-treated patients with an incidence between 1% and 5%. In descending order of frequency they were: anorexia, nervousness, insomnia, fever, confusion, diarrhea, abdominal pain, dyspnea, tachypnea, asthenia, dyspraxia, postural hypotension, sinus tachycardia, tachycardia, asthenia, abdominal pain, thought disorders, and hiccups.

The following adverse reactions occurred in less than 1% of patients involved in clinical trials or were reported in postmarketing surveillance: acute myeloid leukemia, chest pain, facial edema, malaise, neck pain, and symptoms associated with either an anginal or anginal-equivalent reaction.

Cardiovascular: angina, syncope, vasodilation, ST depression.
Dyspnea: dyspnea, apnea, tachypnea, gastrointestinal distress, increased appetite, nausea and vomiting, stomatitis, etc.

Hemic and Lymphatic: lymphadenopathy.
Metabolic and Nutritional: dehydration, edema, hypothermia, peripheral edema, syndrome of inappropriate antidiuretic hormone secretion, thirst.

Nervous: abnormal gait, agitation, anorexia, depersonalization, depression, emotional lability, hallucinations, hyperkinesia, hypokinesia, hypotonia, peripheral neuropathy, speech disorders, stupor, tremor, tinnitus, withdrawal syndrome with or without alterations.

Respiratory: cough, increased sputum, weight reduction.
Special Senses: abnormal vision, taste perversion.

Urogenital: abnormal menses, decreased libido, dysuria, hematuria, impotence, polyuria, urinary retention, urinary incontinence.

OVERDOSEAGE: Acute overdose with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death.

Deaths due to overdose have been reported with abuse and misuse of OxyContin by crushing, injecting, or crushing the crushed tablets. Review of case reports has indicated that the risk of fatal overdose is further increased when OxyContin is abused concurrently with alcohol or other CNS depressants, including other opioids.

One of the treatment of oxycodone overdose, primary attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. Supportive measures (including oxygen and resuscitation) should be employed in the management of cardiac and pulmonary arrest accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

The pure opioid antagonists such as naloxone or nalmefene are specific antidotes against respiratory depression from opioid overdose. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose. In patients who are physically dependent on any opioid agonist, including OxyContin, an abrupt or complete removal of opioid effects may precipitate an acute abstinence syndrome. The severity of the withdrawal syndrome produced will depend on the degree of physical dependence and the dose of the antagonist administered. Please see the prescribing information for the specific opioid antagonist for details of their proper use.

Managing Expected Opioid Adverse Experiences: Most patients receiving oxycodone, especially those who are opioid-naïve, will experience side effects. Frequently the side effects from OxyContin are transient, but may require evaluation and management. Adverse events such as constipation should be anticipated and treated aggressively and prophylactically with a standard laxative and/or stool softener. Patients do not usually become tolerant to the constipating effects of opioids.

Some opioid-related side effects such as sedation and nausea are usually self-limiting and often do not persist beyond the first few days. If nausea persists and is unacceptable to the patient, treatment with anti-nausea or other modalities may relieve these symptoms and should be considered.

Patients who receive OxyContin may pass an amount called "spoil" in the stool or in vomitus. These ghosts contain little or no residual oxycodone and are of no clinical consequence.

SAFETY AND HANDLING: Oxycodone is a Schedule II controlled substance that contains oxycodone which is a controlled substance. Like morphine, oxycodone is controlled under Schedule II of the Controlled Substances Act.

OxyContin has been targeted for theft and diversion by criminals. Healthcare professionals should contact their State Professional Licensure Board or State Controlled Substances Authority for information on how to prevent and detect abuse or diversion of this product.

Store at 20°C (77°F); excursions permitted between 15°C-30°C (59°-86°F). Healthcare professionals can dispense Purdue Pharma's Medical Services Department (1-888-726-7538) for information on this product.

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Purdue Pharma L.P., Stamford, CT 06901-3431

U.S. Patent Numbers: 4,931,546; 4,970,075; 5,266,331; 5,508,024; 5,549,912; and 5,656,295.
DS08689
July 30, 2003

OXYCONTIN (oxycodone HCl controlled-release) TABLETS. 10 mg 20 mg 40 mg 80 mg 160 mg. Brief summary of prescribing information for complete prescribing information please see package insert.

INDICATIONS AND USAGE: OxyContin is a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

CONTRAINDICATIONS: OxyContin is contraindicated in patients with known hypersensitivity to oxycodone, in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or of moderate respiratory depression) and patients with acute or severe bronchial asthma or emphysema.

WARNINGS: OXYCONTIN TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OXYCONTIN TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.

Interactions with Alcohol and Drugs: Oxycodone may be expected to have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

ADVERSE REACTIONS: OxyContin may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.

The administration of oxycodone may obscure the diagnosis or clinical course in patients with acute abdominal conditions. Oxycodone may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings.

Interactions with CNS Depressants: Oxycodone should be used with caution and started in reduced dosage (1/2 to 1/3 of the usual dosage) in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, other tranquilizers, and alcohol.

Interactions with Mixed Agonist/Antagonist Opioid Analgesics: Agonist/antagonist analgesics (i.e., pentazocine, nalbuphine, and buprenorphine) should be administered with caution to patients who are concurrently receiving OxyContin.

Abuse and Potential for Dependence: Oxycodone is a Schedule II controlled substance with an abuse liability similar to morphine and is subject to criminal diversion.

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